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# DATA EVALUATION RECORD - SUPPLEMENT

PARAQUAT DICHLORIDE

Study Type: §82-4, Subchronic Inhalation Toxicity Study in Rats

Work Assignment No. 3-01-88 C (MRID 00113718)

Prepared for
Health Effects Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
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Prepared by
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Disclaimer

This Data Evaluation Record may have been altered by the Health Effects Division subsequent to signing by Dynamac Corporation personnel.

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Template version 11/01

**DATA EVALUATION RECORD - SUPPLEMENT**

TXR# for previous review was not provided

This supplement contains:
-New cover sheet
-New executive summary
-Revised classification statement

**STUDY TYPE:** Subchronic Inhalation Toxicity in Rats; OPPTS 870.3465 [§82-4]; OECD 413

**PC CODE:** 061601 **DP BARCODE:** D321791
**TXR#:** 0053747

**TEST MATERIAL (PURITY):** Paraquat dichloride (approximately 40% w/w paraquat cation)

**SYNONYMS:** 1,1'-dimethyl-4,4'-bipyridinium dichloride

**CITATION:** Hardy, C.J., P. Grimshaw, L.M. Cobb, *et. al.* (1979) Three week inhalation study in rats exposed to an aerosol of paraquat. Huntingdon Research Center, Huntingdon, Cambridgeshire, England. Laboratory Study/Report No.: ICI 254 7949, June 8, 1979. MRID 00113718. Unpublished.

**SPONSOR:** ICI Central Toxicology Laboratory, Alderley Park, Macclesfield, Cheshire, England

**EXECUTIVE SUMMARY** - In a subchronic inhalation toxicity study (MRID 00113718), Sprague-Dawley rats were exposed by whole body inhalation to paraquat dichloride (approximately 40% paraquat ion) administered as a respirable (particle size < 2 μm) aerosol at nominal concentrations of 0, 0.01, 0.1, 0.5, or 1.0 μg/L paraquat ion (equivalent to analytical concentrations of 0, 0.012, 0.112, 0.487, and 1.280 μg/L, respectively) for 6 hours/day, 5 days/week for 3 weeks. The numbers of rats of each sex assigned to these groups were as follows: 32 (control group); 16 (0.5 μg/L); and 36 (remaining groups). Parameters examined included clinical observations, body weights, food consumption, and water consumption. At the end of the three-week treatment period (15 total exposures), 16 rats/sex from the control group and 8 rats/sex/group from the remaining groups were terminated and examined; 8 rats/sex/group were euthanized and examined after a two-week recovery period. Gross and microscopic examinations were restricted to the respiratory tract (nasal passages, pharynx, tongue, larynx, trachea, and lungs). The remaining rats in the control, 0.01, and 0.1 μg/L groups were euthanized

after the 5th exposure, the 15th exposure, and 1, 2, and 3 days after the 15th exposure for paraquat estimations (Note to EPA reviewer: see Table 1 on page 28 of the study report for details of this study design. This information was not accurately reported in the previous "HED Chapter for the Paraquat RED").

There were no treatment-related effects on body weights, food consumption, water consumption, or gross pathology at any concentration.

The 1.0 µg/L group was not exposed after Day 1 because 28/36 males (78%) and 29/36 females (80%) died from respiratory failure in the subsequent 14 days.

All rats in the 0.1 µg/L group exhibited nasal discharge and squamous keratinizing metaplasia, and/or hyperplasia of the epithelium of the larynx. The changes in the epithelium were still observed in 11/16 (69%) of the rats euthanized at the end of the recovery period.

Additionally in the 0.5 µg/L group, the following findings were observed after 3 weeks: (i) extensive ulceration, necrosis, inflammation and squamous keratinizing metaplasia, and marked/moderate hyperplasia of adjacent epithelia in larynx of all rats; and (ii) aggregations of foamy macrophages in the bronchioles or alveoli, hypertrophy of the epithelium and thickened alveolar walls in the lungs of most or all rats. After the 2-week recovery period, no ulceration or necrosis was observed in the larynx, but changes in the lungs were still seen. In addition, disruption of bronchiolar epithelium, adjacent to the macrophage aggregation, was noted.

At 0.01 µg/L, there were no treatment-related effects on any parameter.

**The LOAEL is 0.10 µg/L based on squamous keratinizing metaplasia and hyperplasia of the epithelium of the larynx. The NOAEL is 0.01 µg/L.**

Note to the EPA reviewer: No memorandum was included with the study indicating that the Agency requested that the study be conducted for three weeks. However, this is the understanding of the Dynamac reviewer based upon personal communication with the Agency.

At the request of the Agency, this study was conducted for a duration of three weeks, instead of the 90 days required by Guideline OPPTS 870.3465. Aside from the different study duration, this study was conducted in accordance with Guideline OPPTS 870.3465.

This 21-day inhalation toxicity study is classified as **acceptable/guideline** and satisfies the guideline requirement (OPPTS 870.3465; OECD 413) for a subchronic inhalation study in the rat.

COMPLIANCE - A signed and dated Quality Assurance statement was provided. Data Confidentiality, Flagging, and GLP Compliance statements were not provided. However, this study was conducted prior to the adoption of GLP standards (CFR 40 Part 160; November 29, 1983).

# DATA EVALUATION RECORD - SUPPLEMENT

FLURPRIMIDOL

Study Type: §84-2, *In vivo* Sister Chromatid Exchange Assay
in Chinese Hamster Bone Marrow

Work Assignment No. 2-01-67 T (MRID 00117937)

Prepared for
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Disclaimer

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**DATA EVALUATION RECORD - SUPPLEMENT**

This supplement contains:
- New cover page
- New executive summary

**STUDY TYPE:** *In vivo* Sister Chromatid Exchange Assay in Chinese Hamster Ovary (CHO) Cells; OPPTS 870.5915 [§84-2]; OECD 479.

**PC CODE:** 125701 **DP BARCODE:** D310483
**TXR #:** 0053007

**TEST MATERIAL (PURITY):** Flurprimidol (96.0% a.i.)

**SYNONYMS:** EL 500; Compound 72500; α-(1-methylethyl)-α-[4-(trifluoromethoxy)phenyl]-5-pyrimidinemethanol

**CITATION:** Kehr, C.C. and S.B. Neal (1982) The effect of EL 500 (compound 72500) on the *in vivo* induction of sister chromatid exchange in bone marrow of Chinese hamsters. Toxicology Division, Lilly Research Laboratories, Greenfield, IN. Laboratory Study No.: 820209SCE, February 1982. MRID 00117937. Unpublished.

**SPONSOR:** Elanco (Eli Lilly Company), Indianapolis, IN.

**EXECUTIVE SUMMARY** - In a mammalian cell cytogenetics assay (sister chromatid exchange, SCE; MRID 00117937), Chinese hamsters (3 females/dose) were treated once via intraperitoneal injection (10 mL/kg) with Flurprimidol (96.0% a.i., Lot #: B14-66F-162) in DMSO/corn oil at doses of 50, 100, 200, or 300 mg/kg at 5 hours after subcutaneous implantation of deoxybromouridine (BUdR; 62.4 mg) tablets. Nineteen hours after treatment, Velban® (1 mg/kg; i.p.) was administered, and 2 hours later the bone marrow was harvested. Cyclophosphamide (12.5 mg/kg) served as the positive control.

Flurprimidol was tested up to cytotoxic concentrations (300 mg/kg). No significant increases in the SCE frequency were observed at any dose. The positive control induced the appropriate response. **There was no concentration-related positive response of SCE induced over background.**

This study is classified as **acceptable/guideline** and satisfies the guideline requirement (OPPTS 870.5900; OECD 479) (sister chromatid exchange assay in CHO cells) for *in vitro* cytogenetic mutagenicity data.

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# R155455

**Chemical:**

**PC Code:**

**HED File Code:** 258 Contractor DER TOX Caution: This Document (review) was completed by a contractor and has not undergone secondary review. This document may not reflect Agency policies.

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